Organelles

Introduction

This lesson is on **membrane-bound organelles**. Membrane-bound means covered in a lipid bilayer, just like the cell itself. We're going to be brief, assuming you've had general biology before, reminding you of what each thing looks like and what it does. We'll cover the nucleus, rough endoplasmic reticulum, Golgi apparatus, vesicles (endosomes and lysosomes), mitochondria, and the smooth endoplasmic reticulum.

Most membrane-bound organelles are found in an elegant arrangement that allows progression from DNA in the nucleus, in the center of the cell, to finished protein product throughout the cell or embedded in the plasma membrane. These organelles are spatially situated within the cell to create a pathway to completion. The nucleus is at the center, containing DNA. DNA is transcribed into messenger RNA (mRNA), which then exits the nucleus. The mRNA immediately encounters the rough endoplasmic reticulum (RER), where protein translation for membrane-bound proteins occurs, progressing as it moves farther and farther from the nucleus. The protein is then sent along microtubules to the Golgi apparatus, where final processing takes place as it moves from the nucleus face of the Golgi (cis) to the cell membrane face of the Golgi (trans). Adequate proteins are then released in vesicles, with some meant to perform destructive functions (lysosomes), while others are meant for export (exocytosis or fusion with the cell membrane). If a membrane-bound vesicle is brought in by endocytosis, it moves in the reverse direction: cell membrane to Golgi, Golgi to the RER.

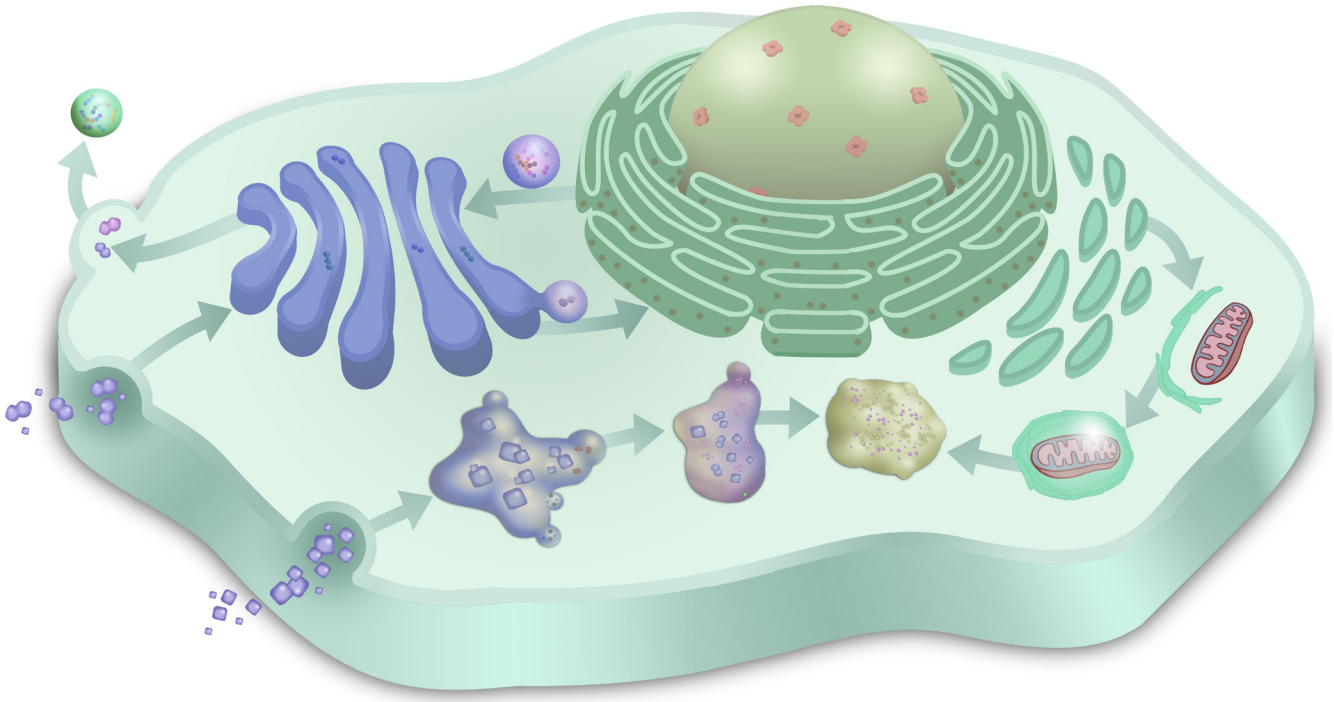


Figure 3.1: Orientation of Organelles within the Cell
The nucleus houses the genetic material, the transcriptional machinery that makes mRNA from DNA, and is in the middle of the cell. DNA is transcribed into mRNA, which leaves the nucleus through pores. Ribosomes on the rough endoplasmic reticulum await the mRNA immediately adjacent to its exit. Translation begins, the simplest form of amino acid sequence nearest the nucleus. As the protein is processed, it gets farther away from the nucleus within the endoplasmic reticulum. Vesicles bud from the endoplasmic reticulum to the Golgi apparatus. There, advanced post-translational modification, sorting, and tagging occur, still farther from the nucleus. The Golgi dispatches vesicles to the membrane or to become lysosomes. The farther from the nucleus, the closer to the plasma membrane, the more sophisticated the product.

While this sorting and exporting function is fairly linear (nucleus, RER, Golgi, vesicle, membrane), there are other organelles acting at the same time, but not in that regionally linear pathway. The mitochondria process oxygen and glucose to make ATP, while the smooth endoplasmic reticulum (SER) helps process lipids.

The Nucleus

The nucleus is surrounded by a **DOUBLE lipid bilayer** called the **nuclear envelope**. The nuclear material is called **chromatin**. Euchromatin is thin, easily accessed DNA that can be replicated or transcribed. Heterochromatin is dense and compressed. Within the nucleus there is also a **nucleolus**, a **small dense area** where **rRNA synthesis occurs** and where cell cycle genes are stored (details of nuclear function in Biochemistry: *DNA to Protein*).

The **outer layer** of the nucleus resembles the endoplasmic reticulum. The **inner layer** is a network of intermediate filaments attached to the **inner lamina**. Basically, the nucleus is surrounded by two layers, one layer that is the plasma membrane of the nucleus, and then another that is the plasma membrane of the endoplasmic reticulum.

DNA is transcribed to mRNA, which immediately leaves the nucleus. Once in the cytoplasm, ribosomes translate the mRNA into protein that will remain in the cytoplasm. That cytoplasm is shielded by the rough endoplasmic reticulum where protein translation can occur within a membrane.

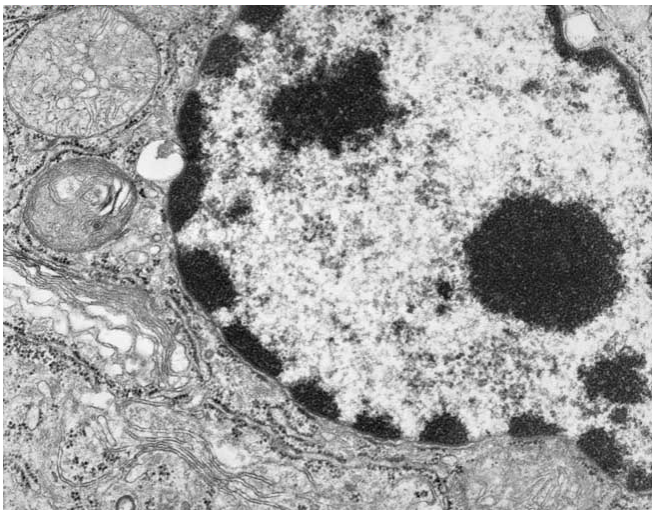


Figure 3.2a: Nucleus and Rough Endoplasmic Reticulum
Electron microscopy of the nucleus showing euchromatin (lightly staining), heterochromatin (darkly staining), the nucleolus (large dense matter in the middle), and the pores, gaps in the plasma membrane.

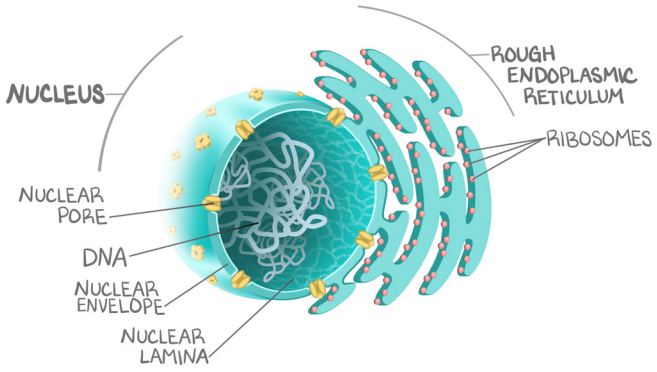


Figure 3.2b: Nucleus
An artist's rendition demonstrating the orientation of DNA in the middle of the cell, RNA exiting the pores, and right to the RER to begin translation. Elegant orientation maximizes efficiency.

Rough Endoplasmic Reticulum (RER)

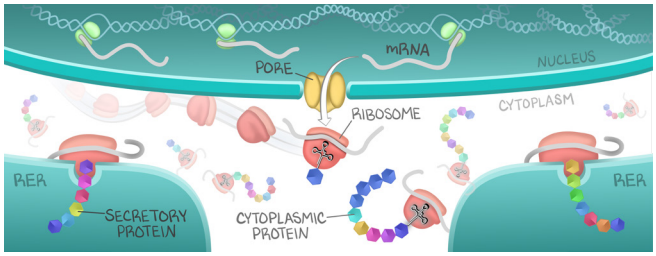
The **rough** endoplasmic reticulum is called rough because of the presence of **ribosomes**. The RER is an active endoplasmic reticulum—the more studded with ribosomes, the more proteins are being translated. This endoplasmic reticulum is made of **plasma membrane**, and is where **vesicular proteins** or **transmembrane proteins** must be synthesized. The ribosomes translate mRNA into protein, which remains in the compartment where it was made. Proteins are large, charged molecules which cannot pass through a plasma membrane. Some proteins ARE the channel for other molecules, so would be too big to have a channel of their own. Being large and polar, the proteins would have a difficult time

getting into or through a lipophilic bilayer of a cell membrane. Therefore, in order to have a protein that spans the membrane, that protein would need to be **built already spanning a membrane**. Whether it's a receptor, pore, or integral protein doesn't matter—the construction of that protein must begin already embedded in the membrane.

The same is true of a protein that is surrounded by a plasma membrane. Fusion with a lysosome (lysosomal enzymes are stored within plasma membrane-bound vesicles) or fusion with the cell membrane (exocytosis) releases the protein contents from within the vesicle. The only way to get a protein to be completely membrane-bound is to have it start surrounded by a lipid bilayer, which means that protein must be **built already inside and surrounded by that membrane**.

The **rough endoplasmic reticulum**, a membrane-bound organelle, is where the ribosomes build these proteins; it is the starting plasma membrane. All protein is built by ribosomes. Some amino acid sequences carry a **signal sequence** that directs the growing amino acid chain and the ribosome to the endoplasmic reticulum. These are destined to be part of a lipid bilayer or to be contained in a vesicle. Those amino acid sequences that lack this signal sequence will be completed in the cytoplasm and must remain there.

All cells make receptors, so all cells need an RER. Cells that are **primarily secretory** are going to have a **robust RER**, such as the β-islet cells of the pancreas, which secrete insulin.



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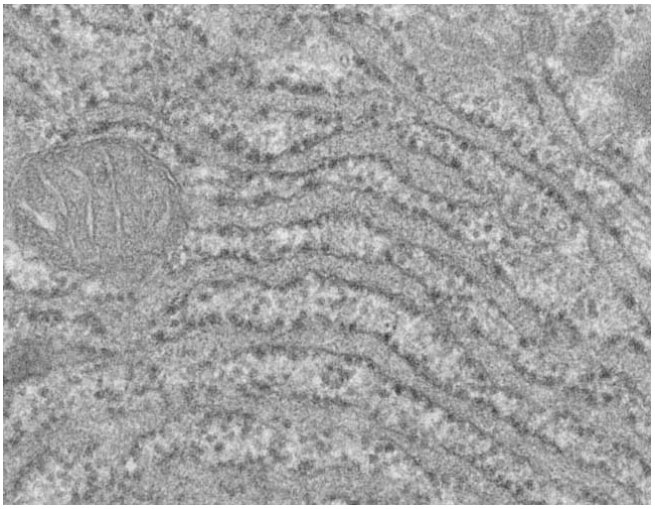


(b)

Figure 3.3: Rough Endoplasmic Reticulum
(a) The rough endoplasmic reticulum is studded with ribosomes and its plasma membrane is continuous with that of the nucleus. Cytoplasmic proteins are translated in the cytoplasm. Vesicular-bound or integral proteins are synthesized in the RER. (b) An electron micrograph of the rough endoplasmic reticulum, again studded with ribosomes.

Golgi Apparatus

While cotranslational modifications do occur in the RER, no protein has completed all of its modifications before leaving the RER. The Golgi apparatus receives vesicles with these "raw" proteins from the RER. As the protein passes through the Golgi, it receives a series of **post-translational modifications**, checks for quality, and designation of destination. Bad proteins can be sent back to the RER. Good proteins are sent forward and eventually leave the Golgi in a vesicle destined for a plasma membrane—usually the cell's plasma membrane or the membrane of a lysosome.

In addition, incoming vesicles carrying the products of **endocytosis**, if not destined for destruction by lysosomes, pass through the Golgi first before being handed down to the RER. The Golgi makes the lysosomes. The Golgi makes the vesicles. The Golgi receives the vesicles from endocytosis.

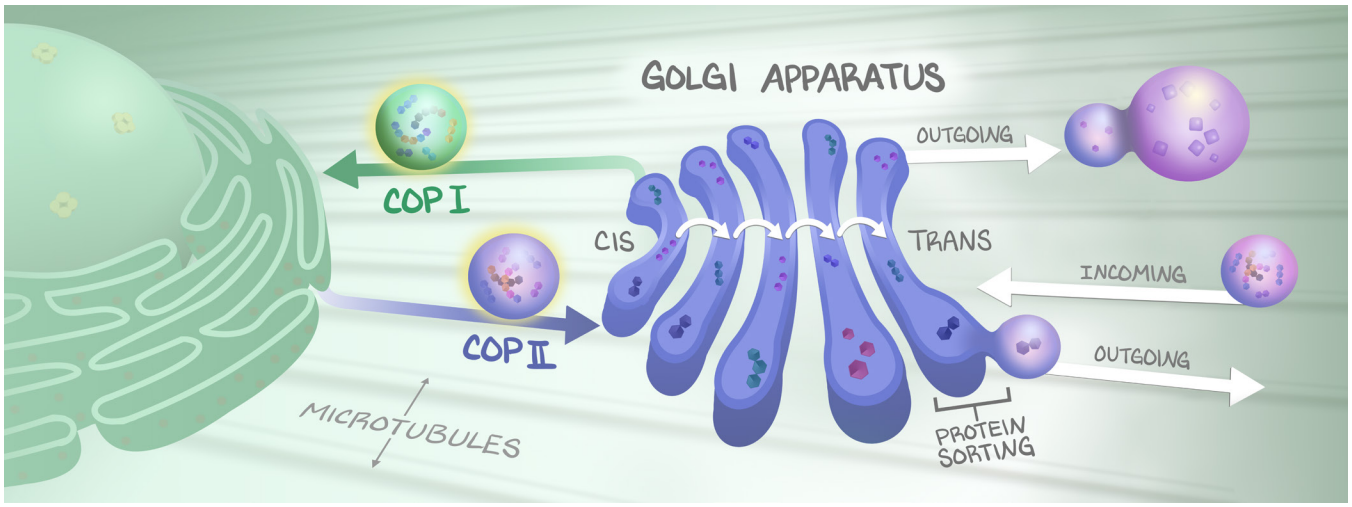


Figure 3.4: Golgi Apparatus
The Golgi apparatus is actually a series of membrane-bound organelles that sort and complete post-translational modification of proteins that are embedded in the membrane or are membrane-bound. Vesicles bud from organelles with plasma membranes, are escorted along microtubules, then fuse with organelles with plasma membranes. COP1 is the vesicle coating that determines directionality "towards the nucleus," or trans-facing; COP2 is the vesicle coating that directs "towards the cell membrane," or cis-facing.

The Golgi apparatus, named before we had electron microscopy, is actually not one singular organelle. It's an arrangement of many layers of self-contained cisternae with dilated edges, interconnected by microtubules. Vesicles are passed back and forth from the RER-facing cis-Golgi to the plasma-membrane-facing trans-Golgi.

COP2 directs vesicles, carried along microtubules, through the Golgi towards the plasma membrane. Outgoing vesicles destined for the cell membrane either carry proteins for excretion (**exocytosis**) or they carry **transmembrane proteins** to be entered into the plasma membrane. **COP1** directs vesicles from the Golgi towards the nucleus.

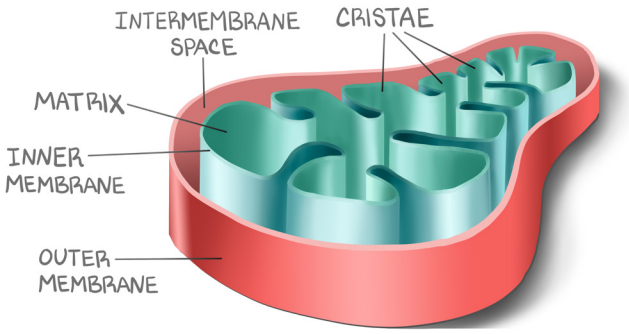
Vesicles/Endosomes/Lysosomes

The Golgi's membrane buds off to form vesicles. These vesicles are carried by proteins that walk along microtubules, moving the vesicles between compartments of the Golgi and throughout the cell (see #4: *Cytoskeleton*). The Golgi finishes the processing of proteins, determines their destination, and sets them on their way.

Some vesicles will **undergo exocytosis**, and their contents will be expelled. Some vesicles will be fused with the cell membrane. Still others are full of toxic enzymes meant for digestion and become **lysosomes** waiting for endocytosis to bring them things to digest. Vesicles brought into the cell from the outside are known as **endosomes**. So, to be clear, vesicles are membrane-bound pools of something that have different names based on their origination and contents.

Mitochondrion

Mitochondria are bean-shaped organelles with a double lipid bilayer. The innermost layer has folds, known as cristae, which often make it the easiest organelle to spot on an electron micrograph. The mitochondrion is the site for **oxidative phosphorylation** (where pyruvate is turned into acetyl-CoA and burned to CO_2 in the citric acid cycle, and also where the electron transport chain harnesses H^+ to make ATP). The mitochondrion is where ketones are made in the liver and used by all other cells that have mitochondria (except RBCs). The mitochondrion also holds the key to **apoptosis**. Mitochondria have their **own mitochondrial DNA**. While technically foreign organelles, with their own DNA and clear separation with two bilayers, the mitochondria are what permit life (glycolysis and aerobic metabolism) and also what regulate cell life (apoptosis).



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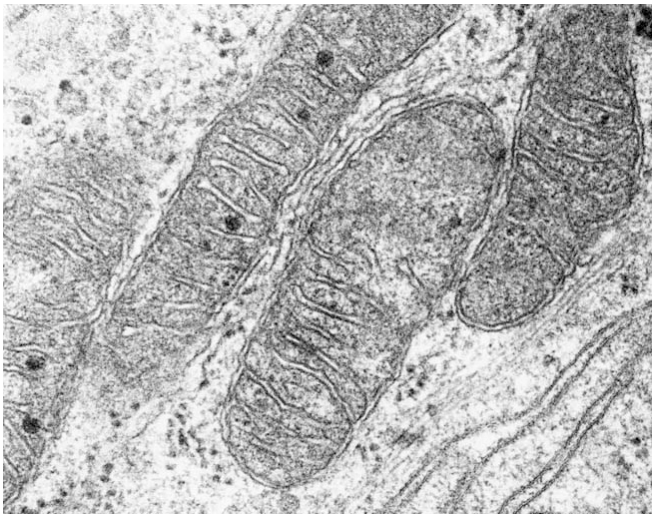

(b)

Figure 3.5: Mitochondrion
(a) Mitochondria are symbiotic organelles—all human cells have them (except red blood cells), but they are truly isolated from our own cytoplasm, more protected than the nucleus. They have two distinct plasma membranes, two distinct lipid bilayers. The outer layer is separated from the inner layer by an intermembrane space. These bean-shaped structures have cristae and cisternae which make them easily identifiable. (b) Electron microscopy of a mitochondrion.

Smooth Endoplasmic Reticulum

The smooth endoplasmic reticulum (SER) is called "smooth" because it looks like the RER but has no ribosomes. But be cautious—the similar appearance of the SER and RER implies similar function, but this is not the case. The SER is designed to manage **lipophilic molecules**, synthesizing lipophilic molecules for excretion and metabolizing lipophilic molecules delivered to the cell. The smooth endoplasmic reticulum is abundant in **hepatocytes**, which not only detoxify lipid-soluble drugs but also are the place where **phospholipids** and **fatty acids** are synthesized.

In **skeletal muscle** the smooth endoplasmic reticulum is the calcium-storing center called the **sarcoplasmic reticulum**.

Citations

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